Remarks

Reconsideration and withdrawal of the rejections of the claims, in view of the remarks presented herein, is respectfully requested. The amendments have been made to clarify the claims in order to expedite prosecution of the present application, and not for reasons of patentability. Therefore, the amendments are not intended to limit the scope of equivalents to which any claim element may be entitled. The amendments to the claims are fully supported by the specification as originally filed.

Removal of the Finality of Office Action is Requested

The Examiner is respectfully requested to remove the finality of the present rejection. The present action is the second Office Action issued in the prosecution of the above-identified application. Pursuant to M.P.E.P. § 706.07(a), the issuance of a final Office Action is only proper under the following two circumstances: (i) when it is necessitated by applicant's amendment of the claims, or (ii) when it is based upon information submitted in an information disclosure statement (IDS) filed during the period set forth in 37 C.F.R. § 1.97(c) with the fee set forth in 37 C.F.R. § 1.17(p). M.P.E.P. § 706.07(a). On page 6 of the Office Action, the Examiner asserts that (i) above, applies to the present action, thus warranting issuance of the final Office Action. However, the Examiner is respectfully requested to consider that the amendments to the claims presented in the previously filed amendment, *i.e.*, the Amendment and Response filed January 9, 2002, did not alter the scope of the pending claims. The amendments to the claims in the Amendment and Response filed January 9, 2002 were presented to (a) remove a parenthetical term, as requested by the Examiner; (b) correct typographical errors; and (c) recite proper antecedent basis. As the present final Office Action is not based upon information submitted in an IDS or necessitated by applicant's amendment of the claims, the Examiner is urged to consider that the finality is improper. Thus, Applicant respectfully requests that the finality of the Office Action be withdrawn.

The 35 U.S.C. § 102(e) Rejection

The Examiner rejected claims 4, 6-10, 13 and 24 under 35 U.S.C. § 102(e) as being anticipated by U.S. Patent No. 6,197,789 (Grainger *et al.*). Claims 4, 13 and 24 have been cancelled, rendering the rejection to claims 4, 13 and 24 moot. Claim 23, upon which claims 6-10 depend, has been amended to no longer be dependent upon claim 4, thus overcoming this rejection of claims 6-10. Withdrawal of the 35 U.S.C. § 102(e) rejection is respectfully requested.

The 35 U.S.C. § 103(a) Rejection

The Examiner rejected claims 1, 3 and 11 under 35 U.S.C. § 103(a) as being unpatentable over Grainger *et al.* Claim 3 has been cancelled, rendering this rejection to claim 3 moot. As these rejections may be maintained with respect to the pending claims, they are respectfully traversed.

The Examiner asserts that Grainger *et al.* teach that Applicant's active agent is useful to inhibit endothelial cell activation (page 3 of the Office Action). The Examiner thus concludes that the art worker would be "motivated to employ Applicant's active agent to reduce or inhibit any activation of endothelium." In addition, the Examiner asserts, regarding claim 11, that the art worker would be motivated to incorporate an anti-diabetes agent, an anti-hypertension agent, an anti-coronary artery disease agent, and an anti-restenosis agent with the active agents of Grainger *et al.* to reduce the sensitivity of endothelially-compromised vascular smooth muscle in a patient in need of such reduction (page 5 of the Office Action).

As amended, claim 1 is directed to a method to normalize the contractile response of an endothelially-compromised vascular smooth muscle cell to a vasoconstrictor agonist in a patient in need of such normalization, comprising administering a pharmaceutically effective amount of a CLC3 blocker, or a pharmaceutically acceptable salt thereof. Claim 11 is directed to such a method, further comprising administering a pharmaceutically-effective compound selected from the group consisting of an anti-diabetes agent, an anti-hypertension agent, an anti-coronary artery disease agent, and an anti-restenosis agent.

Grainger *et al.* relate a therapeutic method for preventing or treating a cardiovascular or vascular indication characterized by a decreased lumen diameter, wherein a therapeutic agent that elevates the level of TGF-beta is employed (column 2, line 37 to column 3, line 2 and column 10, lines 44-46). Grainger *et al.* disclose that such an agent can inhibit the activity of a VSCM, such as proliferation, contraction, and migration (column 17, lines 41-48) as well as inhibit the "pathological" or "abnormal" activity of VSCM (column 3, lines 17-22 and column 6, lines 15-16), which is defined by Grainger *et al.* as "division, growth or migration of cells occurring more rapidly or to a significantly greater extent than typically occurs in a normally functioning cell of the same type, or in lesions not found in healthy tissues" (column 7, lines 61-65). However, there is nothing in Grainger *et al.* that teaches or suggests the normalizing the contractile response of an endothelially-compromised vascular smooth muscle cell to at least one vasoconstrictor agonist.

The Examiner is urged to consider that the "inhibition" of VSCM activity is not the equivalent of smooth muscle cell "normalization." Applicant submits that a "new use" of a composition is clearly patentable subject matter under 35 U.S.C. § 100(b). The present claims are directed to previously unknown uses for CLC3 blockers, *e.g.*, tamoxifen, which are based on the discovery that, *inter alia*, tamoxifen normalizes the increased sensitivity to vasoconstrictor agonists that is associated with endothelially-compromised smooth muscle, *i.e.*, smooth muscle having a damaged or disrupted endothelial layer. To render such a claim obvious, the obviousness of the claimed result must be apparent to one of skill in the art from the prior art, viewed without the benefit of knowledge of Applicant's invention. Thus, even if tamoxifen has been reported to "inhibit" vascular smooth muscle cell contraction, there is nothing in the cited art to suggest that it can correct or normalize the effect of vasoconstrictor agonists on endothelially-compromised VSMC. Therefore, Grainger *et al.* do not obviate the pending claims, and Applicant respectfully requests that the 35 U.S.C. § 103(a) rejection be withdrawn.

Conclusion

Applicant respectfully submits that the claims are in condition for allowance and notification to that effect is earnestly requested. The Examiner is invited to telephone Applicant's attorney (612 373-6961) to facilitate prosecution of this application.

If necessary, please charge any additional fees or credit overpayment to Deposit Account No. 19-0743.

Respectfully submitted,

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The undersigned hereby certifies that this correspondence is being transmitted by facsimile (FAX NO. 703-308-7924) to: Box AF, Commissioner of Patents, Attn.: Examiner Jennifer Kim, GAU 1617, Washington, D.C. 20231 on this 30 day of October, 2002.

Candis B. Buending
Name

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Signature